



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of :

Maurizio Valleri & | Examiner : Pulliam, Amy E.  
Alessandro Tosetti |  
Serial No. 09/463,586 | Art unit : 1615  
filed on April 24, 2000 |  
Pharmaceutical compositions containing |  
Vitamin D and calcium, their preparation and |  
Therapeutic use |

DECLARATION UNDER 37 CFR 1.132

I, Maurizio VALLERI, declare that:

1. I am an Italian citizen residing in Florence ITALY
2. I am familiar with the English language.
3. I further declare that:
  4. I graduated in "Pharmaceutical Chemistry and Technology" at the University of Florence, Italy, in 1982. and have achieved specialization in "Industrial Pharmacy" at the University of Pavia, Italy.
  - 5 I have attended intensive professional courses in "Pharmaceutical process development", Amsterdam 1996  
"Pilot plant studies and process scaling", Amsterdam 1997  
"Powders: their properties and processing"; Amsterdam 2003
  6. At the present time, I am responsible for process transfer technology. in the galenic department of A. Menarini Manufacturing Logistics and Services, Florence Italy
  7. I further declare the following experiments were carried out under my direct supervision: Sachets were prepared using the procedures disclosed in the above identified application where

Vitamin D as Vitamin D3 in the range of 500-1000IU and calcium phosphate in the amount of 1-2g were granulated using each of the polymeric binders set forth in Table 1:

TABLE 1

Polymer used	Method	Amount (mg) / sac	Results
<u>1. polyvinyl pyrrolidone</u>	Wet granulation	50	No granules formation No flowability improvements
<u>2. polyvinyl pyrrolidone</u>	Wet granulation	100	Some hard granules No flowability improvements Bad VitD3 distribution Bad dispersion in water Sandy taste in mouth
3. PEG 6000	Wet granulation	500	Some hard granules Bad dispersion in water Sandy taste in mouth
4. Mannitol	Wet granulation	200	Hard granules Bad dispersion in water Sandy taste in mouth
5. Maltodextrin	Wet granulation	250	Hard granules Bad dispersion in water Sandy taste in mouth
6. Maltodextrin + Na Croscarmellose	Wet granulation	150 + 50	Hard granules Bad dispersion in water Low disintegration
7. Silicon oil	Mixing	500	Good dispersion in water Unpleasant appearance
8. Liquid paraffin	Mixing	500	Good dispersion in water Unpleasant

			appearance Slight unpleasant taste
9. PEG 400	Mixing	800	Good dispersion in water Good appearance Acceptable taste
10. Propylene glycol	Mixing	800	Good dispersion in water Good appearance Good VitD3 distribution Acceptable taste
11. Propylene glycol	Mixing	1000	Good dispersion in water Good appearance Good VitD3 distribution Slight bitter

Sac = granulate containing sachet

8. From the above results, it is apparent that tests 7-11, which are according to the invention described in the above identified application, provide granules that provide a good dispersion in water. In addition, tests 9-11 provide exceptional compositions which have a good appearance as well as good dispersion characteristics in water. The dispersability and the appearance of pharmaceuticals are not predictable and can only be determined after a particular product is made.

9. I further declare that all the statements of my own knowledge are true and that all the statements made on information and belief are believed to be true and further that these statements were made with the knowledge that willful false statement and the like so make are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the Applicant or of any patent issuing thereon.

September 30 2004

Valleri Maurizio

Maurizio Valleri